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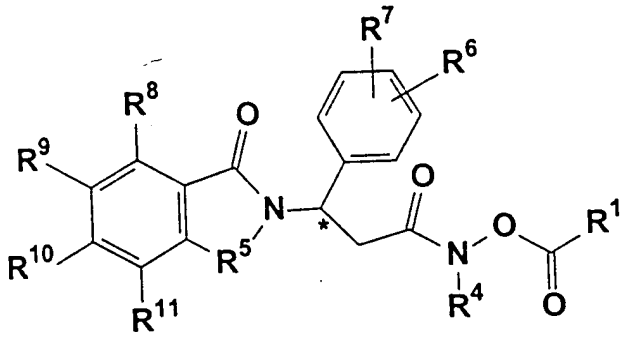
We claim:

1. An acylhydroxamic acid derivative selected from the group consisting of

(a) compounds of the formula:



wherein

the carbon atom designated * constitutes a center of chirality,

R^4 is hydrogen or $-(C=O)-R^{12}$;

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazoyl, imidazolyl methyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein R*and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethlyl, and n = 0, 1, 2;

R^5 is C=O, CH_2, CH_2-CO-, or SO_2;

each of R^6 and R^7, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-indanyloxy, 2-indanyloxy, C_4-C_8-cycloalkylidenemethyl, or C_3-C_{10}-alkylidenemethyl;

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is

(i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo, or

(ii) one of R^8, R^9, R^{10}, and R^{11} is acylamino comprising a lower alkyl, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen, or

(iii) hydrogen if R^8 and R^9 taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(iv) hydrogen if R^{10} and R^{11}, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(v) hydrogen if R^9 and R^{10} taken together are benzo; and

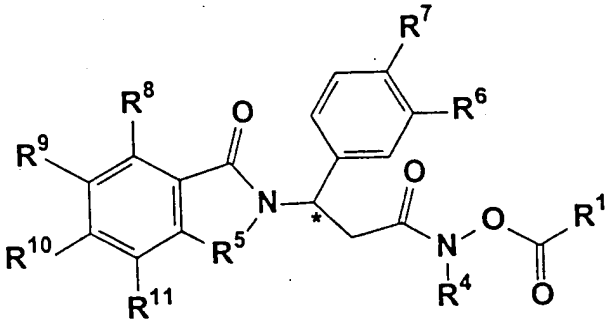
(b) The acid addition salts of said compounds which contain a nitrogen atom capable of being protonated.

2. An acylhydroxamic acid derivative according to claim 1 wherein each of R^8, R^9, R^{10}, and R^{11} is hydrogen, halo, alkyl of 1 to 4 carbon atoms, or alkoxy of 1 to 4 carbon atoms.

3. An acylhydroxamic acid derivative according to claim 1 wherein one of R^8, R^9, R^{10}, and R^{11} is amino, alkyl amino, dialkyl amino, or acyl amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, or hydroxy, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen.

4. An acylhydroxamic acid derivative according to claim 1 wherein R^8, R^9, R^{10}, and R^{11} are hydrogen.

5. An acylhydroxamic acid derivative according to claim 1 wherein said compound has the formula:



in which

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or $-(C=O)-R^{12}$, where

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylmethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein R*and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethlyl, and n = 0, 1, 2;

R^5 is C=O or CH_2;

each of R^6 and R^7, independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms; C_4-C_6-cycloalkylidenemethyl, C_2-C_{10}-alkylidenemethyl, C_6-C_{18}-bicycloalkoxy, C_6-C_{18}-tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy; and

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms

6. An acylhydroxamic acid derivative according to claim 5, wherein each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, alkyl of 1 to 4 carbon atoms, halo, or alkoxy of 1 to 4 carbon atoms.

7. An acylhydroxamic acid derivative according to claim 5 wherein one of R^8, R^9, R^{10}, and R^{11} is acylamino, amino, hydroxy, alkyl of 1 to 10 carbon atoms, and the remaining of R^8, R^9, R^{10}, and R^{11}, are hydrogen.

8. An acylhydroxamic acid derivative according to claim 5, wherein R^8, R^9, R^{10}, and R^{11} are

(a) at least one alkyl of 1 to 10 carbon atoms with the remainder of R^8, R^9, R^{10}, and R^{11} being hydrogen, or

(b) at least one alkoxy of 1 to 10 carbon atoms with the remainder of R^8, R^9, R^{10}, and R^{11} being hydrogen.

9. An acylhydroxamic acid derivative according to claim 5 wherein R^8, R^9, R^{10}, and R^{11} are hydrogen.

10. An acylhydroxamic acid derivative according to claim 5 wherein one of R^8, R^9, R^{10}, and R^{11} is acylamino and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen.

11. An acylhydroxamic acid derivative according to claim 5 wherein two of R^8, R^9, R^{10}, and R^{11} are hydrogen and the remaining of R^8, R^9, R^{10}, and R^{11}, independent of each other, are alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, amino, or acylamino.

12. An acylhydroxamic acid derivative according to claim 5 wherein R^4 is hydrogen.

13. An acylhydroxamic acid derivative according to claim 5 wherein R^4 is $-(C=O)-R^{12}$, and where R^{12} is a lower alkyl of 1 to 6 carbon atoms.

14. An acylhydroxamic acid derivative according to claim 5, wherein

R^4 is hydrogen;

R^5 is C=O;

R^8 is hydrogen; and

one of R^9 and R^{11} is hydrogen and the other of R^9 and R^{11}, taken together with R^{10}, is benzo.

15. An acylhydroxamic acid derivative according to claim 5, wherein

R^4 is hydrogen;

R^5 is C=O;

R^8 and R^9 are hydrogen; and

R^{10} and R^{11}, taken together, are methylenedioxo or dialkoxyl.

16. An acylhydroxamic acid derivative according to claim 5, wherein

R^7 is methoxy; and

R^6 is ethoxy, cyclopentoxy, or isopropoxy.

17. An acylhydroxamic acid derivative according to claim 5 wherein R^6 and R^7 are independently of each other, alkoxy or 1 to 10 carbon atoms, cycloalkoxy, or bicycloalkoxy.

18. An acylhydroxamic acid derivative according to claim 1, which is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

19. A pharmaceutical composition comprising a quantity of an acylhydroxamic acid derivative according to claim 1, which derivative is a substantially chirally pure (R) -isomer, a substantially chirally pure (S)-isomer, or a mixture thereof,

sufficient upon administration in a single or multiple dose regimen to reduce or inhibit levels of TNFα or in a mammal in combination with a carrier.

20. A pharmaceutical composition comprising a quantity of an acylhydroxamic acid derivative according to claim 1, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, sufficient upon administration in a single or multiple dose regimen to inhibit undesirable levels of at least one of matrix metalloproteinases and PDE 4 in a mammal in combination with a carrier.

21. A method of inhibiting undesirable levels of TNFα in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 1, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

22. A method of inhibiting undesirable levels of matrix metalloproteinases in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 1, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

23. A method of treating in a mammal a disease selected from the group consisting of inflammatory disease and autoimmune disease, which comprises administering thereto an effective amount of a compound according to claim 1, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

24. A method according to claim 23 wherein the disease is at least one member selected from the group of arthritis, rheumatoid arthritis, inflammatory bowel

disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host disease, asthma, COPD, psoriasis, atopic dermatitis, Lupus, adult respiratory distress syndrome, and acquired immune deficiency syndrome.

25. A method of treating cancer in a mammal which comprises administering thereto an effective amount of a compound according to claim 1, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

26. A method of treating undesirable angiogenesis in a mammal which comprises administering thereto an effective amount of a compound according to claim 1, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

27. A method of inhibiting phosphodiesterases type IV or PDE 4 in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 1, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

28. An acylhydroxamic acid derivative according to claim 1, wherein the compound is selected from the group consisting of a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, where the isomer is (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) propanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl) propanoylamino) acetate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxy phenyl)propanoylamino) pentanoate; (3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) benzoate; (3-(3-cyclopentyloxy-4-methoxy phenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino) acetate; (3-[4-(acetylamino)-1,3-

dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl) propanoylamino) acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoyl amino) acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; -N-acetyl-3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; N-acetyl-3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisoindolin-2-yl)propanoylamino) acetate; (3-[5-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino) acetate; (3-(1,3-dioxobenzo[e] isoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl) propanoyl-amino) acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-phthalimido-propanoylamino) pyridine-3-carboxylate; (3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino) acetate; (N-acetyl-3-[4-(acetylamino)-1,3-dioxoisoindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl) propanoylamino) acetate; or (3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolin-2-yl)propanoylamino) acetate.

29. An acylhydroxamic acid derivative according to claim 5, which is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

30. A pharmaceutical composition comprising a quantity of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, sufficient upon administration in a single or multiple dose regimen to reduce or inhibit levels of TNFα in a mammal in combination with a carrier.

31. A pharmaceutical composition comprising a quantity of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, sufficient upon administration in a single or multiple dose regimen to inhibit undesirable levels of matrix metalloproteinases or PDE 4 in a mammal in combination with a carrier.

32. A method of reducing or inhibiting undesirable levels of TNFα in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

33. A method of inhibiting undesirable levels of matrix metalloproteinases in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

34. A method of treating in a mammal a disease selected from the group consisting of inflammatory disease and autoimmune disease, which comprises administering thereto an effective amount of a compound according to claim 5, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

35. A method according to claim 34, wherein the disease is at least one member selected from the group consisting of arthritis, rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host

disease, asthma, COPD, psoriasis, stopic dermatitis, Lupus, adult respiratory distress syndrome, and acquired immune deficiency syndrome

36. A method of treating cancer in a mammal which comprises administering thereto an effective amount of a compound according to claim 5, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

37. A method of treating undesirable angiogenesis in a mammal which comprises administering thereto an effective amount of a compound according to claim 5, which compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

38. A method of inhibiting undesirable levels of phosphodiesterase type IV in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

39. A method of treating dermal diseases in a mammal which comprises administering thereto an effective amount of an acylhydroxamic acid derivative according to claim 5, which derivative is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

40. An acylhydroxamic acid derivative according to claim 10 wherein acyl contains a carbonyl group and alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl, imidazolylmethlyl, or $CHR^*(CH_2)_nNR^*R^0$, wherein R*and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl,

benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethlyl,

and n = 0, 1, 2.